LETTERS TO THE EDITOR

Molybdenum in Human Nutrition

To the Editor:

Molybdenum is classified as a trace metal among human nutrients. It is essential for good health, but there is no evidence that molybdenum deficiency is responsible for any human disease.[1] An unequivocal need for growth and maintenance in humans has not been determined.

Molybdenum is a chief constituent of the iron-containing enzyme xanthine oxidase, which breaks down purines to uric acid and is also involved in the mobilization of ferritin, storage iron, from reserves in the liver. Molybdenum is essential for xanthine oxidase activity and also for the actions of the enzymes sulfite oxidase and aldehyde oxidase. Xanthine oxidase catalyzes the transfer of hypoxanthine and xanthine to uric acid. Sulfite oxidase speeds the oxidation of sulfite to sulfate on proteins. And aldehyde oxidase oxidizes and detoxifies certain aldehydes, purine, pyrimidine, and pteridine. Both xanthine oxidase and aldehyde oxidase function in the terminal respiratory chain of oxidative metabolism in conjunction with another of their components, flavin adenine dinucleotide (FAD). Some dehydrogenases and other flavoenzymes containing molybdenum are known in microbes but have not yet been demonstrated in humans. In animals and some plants, molybdenum seems to link flavin nucleotide to protein.

Molybdenum is easily absorbed in the upper small intestine, and is

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transported attached to proteins in blood for tissue storage and use as an enzyme cofactor. The metal is transported to the liver by red blood cells.[2] Concentrations in human whole blood range from 30 to 700 nmol/L and vary with the soil contents of the metal in different geographic areas. Normal values for serum molybdenum levels have not yet been established. Excretion takes place in the bile and urine. Molybdenum is secreted in the bile and then recirculated into the liver by an enterohepatic circulation with the excess appearing in the feces. About half of the total intake may be excreted in the urine. Urinary levels vary with environmental exposure to the metal and do not regulate tissue levels.

There is no storage site for molybdenum in humans, but the highest concentrations are found in the liver, bones, adrenals, kidneys, small intestine, and skin.[3] The molybdenum content of animal organs is extremely low. In humans, the kidney contains about 1.6 parts per million, the liver about 3.29, and spleen, lung, and brain from 0.14 to 0.20.

Molybdenum Requirements. The amount of molybdenum required by humans is not established; there is recommended dietary allowance. The Food and Nutrition Board of the National Academy of Sciences advises that deficiency, although well documented in animals, has never been observed in humans. The Board's estimated safe and adequate dietary intake is 0.15 to 0.50 mg for adults, 0.05 to 0.15 mg for adolescents, and 0.03 to 0.08 mg for infants.[4] The parenteral needs for ammonium molybdenate are from 20 to 30 μg per day, Most physicians will not add molybdenum to the feeding solution for patients on total parenteral nutrition until a definite need is demonstrated.

Dietary Molybdenum. The amount

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of molybdenum in plants depends greatly on the content in the soil, which varies geographically and with soil type. The molybdenum content is low in plants grown in acid, sandy soils and higher in those grown in alkaline or neutral soils with a high proportion of organic matter. Therefore, dietary molybdenum also varies considerably. Average daily intake ranges from 0.1 to 0.46 mg,[5] although extremes range from 0.05 to 0.53 mg daily.[6] The best food sources of molybdenum, with approximately 0.6 parts per million include legumes, whole grains, animal organ meat, dark green leafy vegetables, and milk.

Molybdenum Deficiency. Molybdenum is a copper antagonist.[7,8] Like zinc, excess molybdenum interferes with copper absorption. In livestock, copper and molybdenum prevent the uptake of excessive amounts of each other, but only in the presence of inorganic sulfate. Molybdate absorption is inhibited by sulfate. It is suspected that in the United States, the relatively high copper intake in humans also inhibits both molybdenum and iron absorption. Some members of animal species with a molybdenum-deficient diet do not grow normally. In rats and chickens fed molybdenum-deficient diets, xanthine oxidase activity in the intestine, but not liver, is decreased.[9] Hepatic xanthine oxidase activity may be reduced, however, upon addition of tungsten, a competitive inhibitor of molybdenum, to the animals diets. In goats and minipigs, molybdenum deficiency without tungsten in the diets, produces anorexia, depressed growth and reproduction, elevated copper levels in the liver and brain, and increased mortality. Molybdenum-responsive growth depression in lambs and poultry proves that a reversible, spontaneously developing deficiency syndrome in

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CALENDAR

February 1990
Activities in Honor of Black History Month.

February 16-20, 1990
Region I-NMA Annual Scientific and Business Meeting. Medicine in the Nineties and Beyond. Barbados. Travel plus lodging $799. Call Astral Travel 718-629-2222. For information, call 201-672-7972.

March 2-4, 1990
NMA Board of Trustees. Las Vegas Bally's Casino Resort, Las Vegas, Nevada.

April 27-29, 1990
NMA Board of Trustees. Washington, DC.

May 3-7, 1990
Fifth International Interdisciplinary Conference on Hypertension in Blacks. Longbeach, California. Call 404-589-3810.

May 25-27, 1990
Tentative Date for Annual Meeting of Region II-NMA, Atlantic City, New Jersey.

June 1990
The Volunteer State Medical Association 86th Annual Scientific Session. Memphis, Tennessee. Call 901-527-1153.

July 9-12, 1990
National Assembly on Addictive Disorders: Enlisting Scientific Knowledge in the War on Drugs. Sponsored by the Vesper Society Group, AMA, APHA, and others. Washington, DC area. (Tentative) Call 415-633-0666.

July 28-August 2, 1990
The 95th Annual Convention and Scientific Assembly of the National Medical Association. Bally Grand Hotel, Las Vegas, Nevada.

November 1990
85th Anniversary Banquet of the Provident Clinical Society of Brooklyn. Brooklyn, New York.

FUTURE
July 1991
The 96th Annual Convention of NMA. Indianapolis, Indiana.

July or August 1991
The 6th International Interdisciplinary Conference on Hypertension in Blacks. Brazil.

July 1992
The 97th Annual Convention of NMA. Hawaii.

Send information about coming events for the Calendar to Theresa Greene Reed, MD, MPH, 11516 Patapapsco Dr., Rockville, Maryland 20852 or call 301-468-6830.

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animals exists.[10] Nonetheless, it is neither necessary nor advisable to supplement diets of animals with the metal.

As mentioned, there is no spontaneous molybdenum deficiency syndrome in humans.[11] In various experimental situations, the following signs and symptoms have been reported: tachycardia, night blindness, irritability, headaches, nausea, lassitude and lethargy, coma, decreased xanthine oxidase activity in the intestine and liver, impaired purine metabolism (hypoxanthine and xanthine cannot be converted to uric acid), and abnormal biochemistry of sulfur-containing proteins.

A molybdenum deficiency syndrome in a young man on total parenteral nutrition for 18 months was described.[12] He experienced severe headache, nyctalopia, tachycardia, tachypnea, nausea, vomiting, central scotoma, lethargy, disorientation, and coma. Hypouricemia was marked and accompanied by raised plasma methionine levels. Conversion of sulfite to sulfate was impaired, with accumulation of sulfite, which is toxic to the central nervous system. Urinary excretion as the oxypurines xanthine, and hypoxanthine, was impaired. These metabolic abnormalities were probably secondary to decreased activities of the molybdenum-dependent enzymes, xanthine oxidase and sulfite oxidase. Addition of 300 μg of ammonium molybdenum to the nutritional solution daily corrected the biochemical and clinical finding.

Molybdenum Excess. Dental caries rates are lower in areas where children consume higher amounts of molybdenum.[13] This finding is consistent with a well-established cariostatic effect of the metal in animals. Whether dental caries in children is increased in subclinical molybdenum deficiency is unknown.

Molybdenum toxicity has been reported in one Russian province where an intake of 10 to 15 mg of the

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metal is ingested daily by some of the inhabitants. A syndrome resembling gout develops, along with high uric acid levels in the serum arthropathy, and renal involvement. Serum xanthine oxidase activities, molybdenum levels, and urinary copper excretion are all high.[14] The syndrome only develops when high amounts of molybdenum are consumed with a normal copper intake. When dietary copper is increased, the gout syndrome does not materialize. This is another example of the reciprocal inhibition between the two metals.[14] The relatively higher exposures of molybdenum in the American diet are not believed to increase the incidence of gout, in part because of higher simultaneous copper intake in the United States.

High molybdenum and low copper intake is suspected in some cases of genu valgum, usually caused by fluorosis in central and southern India.[15] Molybdenum increases fluoride absorption and retention in muscle and brain.[16]

Conclusion. Molybdenum is an essential trace element plentiful in food, and a balanced diet will provide all the molybdenum needed for normal function at all levels of activity. Multivitamin supplements commonly contain the metal, typically 15 μg, in the form of yeast, per tablet or capsule. This practice is unnecessary. A high normal daily intake of molybdenum (0.54 mg), compromises copper balance and, therefore, molybdenum supplementation may be harmful.

Calorie-restricted diets are now common in the United States, especially among women. Depending on the severity of restriction, molybdenum deficiency could theoretically develop, although this result is unlikely.

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